UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/931,732	08/16/2001	Bob D. Brown	OASBIO.001C1	4615

20995 7590 10/20/2004

KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
ASHEN, JON BENJAMIN	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/931,732	BROWN ET AL.	
	Examiner	Art Unit	
	Jon B. Ashen	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *06 December 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *13-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/28/02; 10/22/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *PTO-1449: 6/16/03*.

DETAILED ACTION

Election/Restrictions

1. Claims 13-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/062002.

Status of the Application

2. Claims 1-19 are pending. Claims 13-19 are withdrawn (see above). Claims 1-12 are currently under examination.

Priority

3. This application claims the benefit of priority of U.S. provisional application filed 4/08/1999.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 5 (and dependent claim 6) are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 5 recites, "said bases."

However, there is no antecedent basis for this limitation in this claim, rendering this terminology, indefinite.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 1-12 are drawn to a variety of antisense oligonucleotides, each of which "complements at least two RNA molecules of a different sequence". These claims read broadly on a vast number of antisense oligonucleotides that complement any two RNA molecules of a different sequence. The specification as filed, however, provides no definition of what is meant by complementary or of what degree of complementarity is required in the claimed antisense oligonucleotide, within the context of the instant invention, that complements portions of two RNA molecules of different sequence. The disclosure of the specification provides only limited examples of several species of antisense oligonucleotides that complement mRNA molecules of different sequence and

provides no indication of how these species are representative of the broad genus as claimed.

The specification does not provide or point to a specific structure that corresponds with the function of being antisense against at least two RNA molecules of different sequence, as claimed. The specification does not disclose any distinguishing identifying characteristics of the claimed antisense oligonucleotides, that would complement at least two RNA molecules of different sequence and function as an antisense oligonucleotide against both, that would indicate that applicant was in possession of this broadly claimed genus. Additionally, the disclosure of the specification provides no specific guidance as to how one skilled in the art might be reasonably led to a particular species of antisense oligonucleotide that would function commensurate with the scope of the claimed invention, that would be antisense to at least 2 RNA molecules of different sequence that could be any two RNA molecules of different sequence, such that the invention would be complete and ready for patenting. The specification, therefore, does not, provide an adequate written description of the genus of antisense oligonucleotides as claimed, which would indicate that applicant was in possession of said genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2nd 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed (see page 1117). Whether the specification shows that applicant was in possession of the claimed invention is not a

single, simple determination, but rather is a factual determination reached by considering a number of factors. Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.

Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., Pfaff v. Wells Elecs., Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").

An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be

used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described.").

Therefore, Applicant has not provided adequate written description of their invention because Applicant has provided "merely a wish or a plan for obtaining the chemical invention claimed" and has not shown how their invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. What, in particular, is the structure of an antisense oligonucleotide that can be any antisense oligonucleotide that complements any two RNA molecules of different sequence that corresponds with the function of modulating the gene expression of any two RNA molecules of different sequence, for example?

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. In the instant case, the specification as filed indicates that a universal base refers to a moiety that may be substituted for any base, that need not contribute to hybridization but that should not significantly detract from hybridization (pg. 6, specification as filed). The particular meaning of "significantly detract" is not set forth. As interpreted herein, a universal base according to Applicant's definition, encompasses any moiety that can be substituted for any base as long as it does not significantly detract from hybridization and therefore, includes, at least, other modified and non modified nucleobases (as these would not significantly detract from hybridization). In regards to "RNA targeting region," no definition of what is intended by this phrase is provided in the specification as filed. Therefore, any region of any oligonucleotide that has the potential to bind to any RNA is considered to be an RNA targeting region. In light of the above interpretations, the following art is applied.

10. Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Cook et al. (U.S. Patent 5,623,065). Claims 1-8 are drawn to an antisense oligonucleotide that comprises at least one non-naturally occurring backbone linkage that comprises at least one universal and/or degenerate base, that is between 6 and about 50 bases (claim 1),

an antisense oligonucleotide that comprises a first and second non-RNase H recruiting region of between 3 and about 15 bases, an RNase H recruiting region of between 3 and about 15 bases, and a second RNase H recruiting region wherein at least one base is a universal and/or degenerate base (claim 3), an antisense oligonucleotide that comprises a non-RNase H recruiting section and an RNase H recruiting section wherein at least one base is a universal and/or degenerate base (claim 5) and an antisense oligonucleotide that comprises an RNase L recruiting region comprising a 2'-5' adenosine oligomer wherein an RNA targeting region of said antisense oligonucleotide comprises at least one universal and/or degenerate base (claim 7). The antisense oligonucleotides of claims 1, 3, 5 and 7 can have no more than about 50% universal and/or degenerate bases (claims 2, 4, 6 and 8 that depend from claims 1, 3, 5 and 7 respectively). Each of the oligonucleotides of the instant invention claimed in claims 1, 3, 5 and 7 is an antisense oligonucleotide that complements at least two RNA molecules of different structure.

Cook et al. disclose antisense phosphorothioate oligonucleotides that are 17 bases in length (columns 25-26, table 1) that comprise 2'-O-methyl modified sugars of 4-7 bases that flank, on both the 3' and 5' ends, between 3 and 9, 2'-deoxy-erythro-pentofuranosyl nucleotides (SEQ ID NOS: 3-6 in table 1) that are antisense oligonucleotides targeted to the codon 12 point mutation of activated H-ras that comprise at least 1 non-naturally occurring backbone linkage, are between 6 and about 50 bases, that further comprise RNase H recruiting and non-RNase H recruiting regions and sections as claimed. Cook et al. also disclose the preparation of a 20mer

oligonucleotide that comprises a 1st region of 6, 2'-5' linked RNA that is attached to a 2'-deoxy phosphorothioate region of 3'-5' linked DNA 8 nucleotides long and a further 6 nucleotide long region of 2'-5' linkages that are added to complete an oligonucleotide having mixed 2'-5' and 3'-5' linkages. In this embodiment, the prior art antisense oligonucleotide of Cook et al. comprises an RNase L recruiting region (that can be 6, 2'-5' linked RNA nucleotides that can be adenosine) and a non-RNase L recruiting region. Any of the prior art antisense oligonucleotides of Cook et al. can comprise a universal base, for example xanthine (column 5, line 62), which is disclosed without limitation, and can therefore be positioned in the RNA targeting region of an antisense oligonucleotide and used to construct an antisense oligonucleotide comprising no more than about 50% universal and/or degenerate bases. The prior art antisense oligonucleotides of Cook et al., complement two RNA molecules of different sequence in that they are complements of wild type and mutant, activated, H-ras. Therefore, Cook et al. anticipate each and every limitation of the invention as claimed in claims 1-8.

11. Claims 1, 2 and 4-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Torrence et al. (U.S. Patent 5, 583, 032). The invention claimed in claims 1, 2 and 4-8 is set forth in a previous rejection. Torrence et al. disclose a chimeric antisense oligonucleotide that targets PKR mRNA at positions 55-73 from the start codon of the PKR mRNA (SEQ ID NO: 6) that comprises 4, 2'-5' linked adenosines (an RNase L-recruiting region) and an a 3',5' –deoxyribonucleotide antisense sequence (an RNA targeting region) (column 24, example 7). Torrance et al. disclose that possible

antisense moiety constituents can include alpha-deoxynucleotides (universal bases according to Applicant's definition on page 6 of the specification as filed) (column 5, line 61). No limitations are disclosed in regards to the possible antisense moiety constituents of Torrence et al., which can be positioned in the RNA targeting region of an antisense oligonucleotide and used to construct an antisense oligonucleotide comprising no more than about 50% universal and/or degenerate bases. The prior art antisense oligonucleotide of Torrence et al. complements at least two RNA molecules of different sequence in that it complements, at least, both mouse and human PKR mRNA. Therefore, Torrence et al. anticipate each and every aspect of the instantly claimed invention.

12. Claims 1, 2, 7, 8, 11 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Stinchcomb et al. (U.S. Patent 5,646,042). The invention claimed in claims 1-2 and 7-8 is set forth in a previous rejection. Claims 11 and 12 are drawn to a ribozyme comprising an RNA targeting region which comprises at least one universal and/or degenerate bases that complements at least 2 RNA molecules of a different sequence (claim 12) wherein said RNA targeting region comprises no more than about 50% universal and/or degenerate bases. Stinchcomb et al. disclose an antisense oligonucleotide that is an optimal c-myb hammerhead ribozyme that comprises phosphorothioate linkages at the 5' end, that is 37 bases in length, that comprises a 3'-3' abasic deoxyribose (3'-3' linked inverted T) and a 2'-C-allyl U, each of which are considered a universal base as per Applicant's definition on page 6 of the instant

specification, wherein said universal bases comprise no more than about 50% of the RNA targeting region (Fig. 20, brief description of the drawings and Example 14 (at least). The prior art anti-c-myb ribozymes of Stinchcomb et al. are disclosed as active against both human and murine mRNA transcripts (column 14, lines 33-41). Stinchcomb et al. also disclose a ribozyme that targets c-myb site 575 (one of the several ribozymes disclosed that target both human and murine mRNA molecules) that is synthesized with 2-5A moieties at the 5' end (575 active Rz + active P(A)4) (column 28, lines 1-25). Therefore, Stinchcomb et al. anticipate each and every limitation of the invention as claimed in claims 1, 2, 7, 8, 11 and 12.

13. Claims 1-6 rejected under 35 U.S.C. 102(e) as being anticipated by Bennett et al. (U.S. Patent 6,172,216). The invention as set forth in claims 1-6 is described in a previous rejection. Bennett et al. disclose an antisense oligonucleotide targeted to mRNA transcripts of both human bcl-xl and bcl-xs that is SEQ ID NO: 22, a chimeric oligonucleotide "gapmer" that is 20 nucleotides in length and composed of a central gap region consisting of ten 2'-deoxynucleotides which is flanked on both sides by 5 nucleotide wings composed of 2'-0-methoxyethyl nucleotides (a first and second non-RNase H recruiting region that are the 2'-MOE wings and an RNase H recruiting region that is the region of ten 2'-deoxynucleotides). The internucleoside linkages are phosphorothioate throughout. Four cytidine residues (out of a total of 20 residues in the oligonucleotide) in the 2'-MOE wings are universal bases that are 5-methylcytidine

(column 28, example 18). Therefore, Bennett et al. anticipate each and every aspect of the instant claims.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claim 7-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Werther et al. (U.S. Patent 5,929,040) in view of Bennett et al. (U.S. Patent 6,172,216), Torrance et al. (U.S. Patent 5,583,032) and Krupp (1993, reference 82, PTO-1449 filed 8/28/02).

Werther et al. teach the construction of a multivalent antisense molecule that targets at least two insulin growth factor binding proteins (IGFBP) (which encompasses IGFBP-2 and IGFBP-5) (column 3, lines 63-67, column 5, lines 30-35) and a method of inhibiting IGF-I mediated cell proliferation using "a polynucleotide capable of interacting with mRNA directed from two or more of an IFG-I gene, an IFG-I receptor gene or a gene encoding an IFGBP such as IGFBP-2 and/or IGFBP-3 (column 4, lines 10-15). The prior art antisense oligonucleotide of Werther et al. is preferably 20-25 nucleotides in length (column 3, lines 34-35) and can be a ribozyme that targets one or more IGFBPs such as IGFBP-2 and/or IGFBP-3 (column 4, lines 40-45) and may be constructed with a non-ionic or phosphorothioate backbone (column 3, lines 55-57). Werther et al. teach benefit of targeting IGFBPs for ameliorating the effects of a proliferative and/or inflammatory skin disorder in a mammal because, "targeting these molecules (*IGF-I, IGF-I receptor and IGFBPs*) according to the methods contemplated herein provides the best results to date" (column 2, lines 35-39)

Werther et al. do not teach universal and/or degenerate bases, RNase H and non-RNase H recruiting regions, RNase L recruiting regions or RNase P recruiting regions.

Bennett et al. teach universal bases that can be included in antisense oligonucleotides, including xanthine (column 8, lines 47-68 bridge to column 9, lines 1-18) and that "Certain of these nucleobases are particularly useful for increasing the binding affinity of the oligomeric compounds of the invention" (column 9, lines 5-7). Bennett et al. also teach chimeric oligonucleotides that are gapmers comprising

modifications that are RNase H and non-RNase H recruiting regions that are "an additional region of the oligonucleotide that may serve as a substrate for enzymes capable for cleaving RNA:DNA or RNA:RNA hybrids" (column 10, lines 16-18). Bennett et al. teach the benefits of these modified regions wherein they recite, "Activation of RNase H, therefore, results in cleavage of the RNA target, thereby greatly enhancing the efficiency of the oligonucleotide inhibition of gene expression" (column 10, lines 20-23).

The teachings of Torrance et al. are set forth previously in this rejection. Torrance et al. also teach that "targeting of a molecule of RNA for cleavage by a ribonuclease has as well been found to be necessary for the specific cleavage of that molecule of RNA" (column 26, lines 29-31) and that "These results are significant in that they show that 2-5A greatly enhances the ability of an antisense oligonucleotide to inhibit specific gene expression. Furthermore, these findings also show that the methods of the present invention are effective against a natural mRNA species in intact cells. Significantly, no special techniques were required for introducing the oligonucleotides into the cells" (column 33, lines 28-35) and that "Because 2-5A-dependent RNase is believed to be present in most mammalian cells, the therapeutic control of protein translation for the treatment of cancer, viral infections, genetic diseases, osteoarthritis, rheumatoid arthritis, restinosis, and a variety of other medical conditions can be accomplished using this technology" (column 34, lines 62-67).

Krupp teaches that advantages of RNase P in antisense applications wherein he recites, "[t]he RNase P approach can combine attractive features from both established

systems: similar to ribozyme systems the free choice between extracellular addition of oligoribonucleotides or intracellular production of RNA transcripts; like the RNase H approach, it takes advantage of the efficiency of a normal cellular enzyme" (pg. 136, column 2, 3rd paragraph) and "RNase P combines the advantages of a ubiquitous cellular enzyme (like RNase H) with the possible choice between short, synthetic antisense oligoribonucleotides and large, in vivo RNA transcripts (like hammerhead ribozymes)" (pg. 138, conclusions, 1st paragraph).

It would have been obvious to one of ordinary skill in the art to construct the a modified multivalent antisense oligonucleotide of Werther et al. that comprised a universal and/or degenerate base, that further comprised RNase H recruiting and non-recruiting regions as taught by Bennett et al. or an RNase L recruiting region as taught by Torrance et al. or an RNase P recruiting region as taught by Krupp in order to provide a multivalent antisense oligonucleotide that was more efficient at degrading target mRNA such that a more effective treatment of disease (proliferative or skin disorders) related to multiple RNA transcripts could be effected.

One of ordinary skill in the art would have been motivated to construct a multivalent antisense oligonucleotide comprising RNase recruiting regions because targeting multiple mRNA transcripts with a single oligonucleotide (for example,IGFBP molecules) was well known in the art and because modifications to antisense oligonucleotides comprising the addition of a universal and/or degenerate bases further comprising an RNase H recruiting and non-recruiting region or an RNase L or RNase P recruiting region were known in the art to provide the benefits of increased duplex

stability as well as to operate by recruiting a naturally occurring enzyme such as an RNase H, L or P to greatly enhance the efficiency of the multivalent oligonucleotide to inhibit gene expression via the degradation of multiple target mRNA transcripts.

One of ordinary skill in the art would have expected success in constructing the above multivalent oligonucleotide comprising a universal and/or degenerate base that further comprised an RNase H recruiting and non-recruiting region or an RNase L or RNase P recruiting region because the prior art shows the success of antisense oligonucleotide therapy using unmodified multivalent antisense oligonucleotides and each of the modifications taught by the prior art, as disclosed above, were known to be effective at enhancing the therapeutic effect of particular antisense oligonucleotide treatments.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

17. No claims currently under examination in this application are free of the prior art searched or in condition for allowance.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon B. Ashen whose telephone number is 571-272-2913. The examiner can normally be reached on 7:30 am - 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jba

SEAN McGARRY
PRIMARY EXAMINER
1635